

Part B:

The objective of the study was to evaluate the equivalence of once a day, two times a day and three times a day dosing of the polymer from Part A of this example. After a four day period to control diet, 12 healthy volunteers were randomized in an open-label, multiple-dose crossover study. The polymer was administered orally as an aqueous suspension of 30 grams (g) once a day for six days, 15 g twice a day for six days, and 10 g three times a day for 6 days in a randomly assigned order based upon 1 of 6 dosing sequences. Laboratory and adverse event assessments were performed throughout the study to monitor safety and tolerability. Subjects were required to consume a controlled diet for the duration of the study. Feces and urine were collected over 24 hour intervals on certain study days to assess potassium excretion.

Subjects were healthy adult males or females without a history of significant medical disease, 18 to 55 years of age, with a body mass index between 19 and 29 kg/m² at the screening visit, serum potassium level >4.0 and ≤5.0 mEq/L, and serum magnesium, calcium, and sodium levels within normal range. Females of childbearing potential must have been non-pregnant and non-lactating and must have used a highly effective form of contraception before, during, and after the study.

Multiple-dose administration of 30 g polymer for 6 days each as either 30 g once daily, 15 g twice daily or 10 g three-times daily, respectively was well tolerated. No serious adverse events were reported, and all adverse events were mild or moderate in severity. An effect was apparent for fecal and urinary excretion of potassium.

For fecal potassium excretion, the mean daily values and change from baseline values were significantly increased for all three dosing regimens. The volunteers receiving the polymer once per day excreted 82.8% of the amount of fecal potassium as those volunteers who received substantially the same amount of the same polymer three-times per day. It is also shown that volunteers receiving the polymer twice per day excreted 91.5% of the amount of fecal potassium as those volunteers who received substantially the same amount of the same polymer three-times per day. For urinary potassium excretion, the mean daily values and change from baseline values were significantly decreased for all three dosing regimens. Surprisingly, there was no statistically significant difference between the three dosing regimens.

Regarding tolerability, 2 of the 12 subjects receiving once a day dosing or twice a day dosing reported mild or moderate gastrointestinal adverse events (including flatulence, diarrhea, abdominal pain, constipation, stomatitis, nausea and/or vomiting). Also, 2 of 12 subjects reported mild or moderate gastrointestinal adverse events on the baseline control diet. Thus, less than 16.7% of these subjects reported mild or moderate gastrointestinal adverse events, an indication that, as used herein, dosing once or twice a day was well tolerated. None of the subjects reported severe gastrointestinal adverse events for any of the dosing regimens or at baseline.

Part C:

Another study was performed to assess the safety and efficacy of a binding polymer that was the same as described above in Part A of this example, but without the sorbitol loading. Thirty-three healthy subjects (26 male and 7 female) between the ages of 18 and 55 years received single and multiple doses of polymer or placebo in a double-blind, randomized, parallel-group study. Eight subjects each were randomly assigned to one of four treatment groups receiving polymer or matching placebo. The subjects received 1, 5, 10, or 20 g of polymer or placebo as a single dose on study day 1, followed by three times daily dosing for eight days following

seven days of diet control. Subjects were required to consume a controlled diet for the duration of the study.

The polymer was well-tolerated by all subjects. No serious adverse events occurred. Gastrointestinal adverse events reported were mild to moderate in severity for one subject. There was no apparent dose response relationship in gastrointestinal or overall adverse event reporting, and no increase in adverse event reports versus placebo.

At the end of the multiple-dose study period, a dose response effect was apparent for fecal and urinary excretion of potassium. For fecal potassium excretion, the mean daily values and change from baseline values were significantly increased in a dose-related manner. For urinary potassium excretion, the mean daily values and change from baseline values were decreased in a dose-related manner.

In comparison of Part C to Part B, those volunteers receiving the same amount of polymer that had the sorbitol loading (Part B) excreted about 20% more potassium in the feces as compared to those volunteers receiving the non-sorbitol loaded polymer (Part C).

When introducing elements of the present invention or the embodiments(s) thereof, the articles “a”, “an”, “the” and “said” are intended to mean that there are one or more of the elements. The terms “comprising”, “including” and “having” are intended to be inclusive and mean that there may be additional elements other than the listed elements.

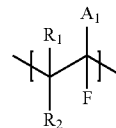
In view of the above, it will be seen that the several objects of the invention are achieved and other advantageous results attained.

As various changes could be made in the above compositions and methods without departing from the scope of the invention, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

What is claimed is:

1. A pharmaceutical composition comprising a crosslinked cation exchange polymer salt loaded with a stabilizing amount of a linear sugar alcohol by slurring in a solution the linear sugar alcohol with the crosslinked cation exchange polymer salt, wherein the stabilizing amount of the linear sugar alcohol is from about 10 wt. % to about 35 wt. % based on the total weight of the composition, and the crosslinked cation exchange polymer salt comprising structural units of Formulae 1 and 2, Formulae 1 and 3, or Formulae 1, 2, and 3, wherein Formula 1, Formula 2, and Formula 3 have the following structures:

Formula 1



Formula 2

